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Original Research Paper

Histopathology

EXTRAUTERINE KERATIN GRANULOMAS: CHALLENGING STAGING OF UTERINE ENDOMETRIOID ADENOCARCINOMA.

Archana N Rijhsinghani*

Consultant, Department of histopathology, agilus Diagnostics Dr Phadke Labs, Udyam, Shivaji Park, Dadar west, Mumbai, Maharashtra,India-400028. *Corresponding Author

ABSTRACT Endometrioid adenocarcinoma constitutes majority of endometrial carcinomas. It shows squamous differentiation and squamous morules on histology. Presence of keratin granulomas in extrauterine sites occur, as keratin materials are speculated to be refluxed from the uterine tumor through the fallopian tubes toward the peritoneum. However, it is important to know that these keratin granulomas in the absence of tumor cells do not have any influence on prognosis or staging of uterine endometrioid carcinoma.

KEYWORDS : Endometrioid Adenocarcinoma, Squamous Differentiation, Keratin Granulomas, Prognosis.

INTRODUCTION

Over 90% of endometrial cancers are epithelial malignancies, in other words, carcinomas. Endometrioid carcinoma histotypes constitute the majority of endometrial carcinomas, and low-grade (FIGO Grades 1 and 2) endometrioid carcinomas account for 80% to 90% of all endometrioid carcinomas, serving as the prototype for the WHO (2014) classification of type 1 endometrial cancers. High-grade serous carcinomas (HGSC) are the prototype for the WHO (2014) classification of type 2 endometrial cancers. About 75% of type 2 endometrial cancers are morphologically high-grade serous (greater than 50%), clear cell (12% to 14%), or undifferentiated (5%) carcinomas.[1]

Squamous differentiation/squamous metaplasia is often associated with endometrial adenocarcinoma and benign lesions, such as endometrial hyperplasia and chronic endometritis.[2]

Case History

52 years/ female, complained of post-menopausal bleeding. Patient underwent dilatation and curettage & was diagnosed as adenocarcinoma on histology. Patient underwent hysterectomy with bilateral salpingo-oophorectomy with bilateral pelvic lymph node dissection. Grossly, a polypoid grey white tumor was seen involving endometrial cavity, measuring 7 x 5 x 2 cms, invading more than half of myometrial thickness, extending to isthmus and endocervix (Figure 1). Grossly bilateral ovaries, fallopian tubes & parametria were unremarkable.

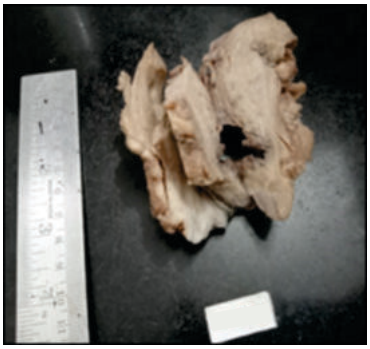

Figure 1: Gross: A polypoid grey white tumor involving endometrial cavity extending to isthmus and endocervix.

On microscopy, section from endometrial tumor revealed moderately differentiated endometrioid adenocarcinoma, FIGO grade 2, invading more than half of myometrial thickness with involvement of isthmus & cervical stroma. Serosa & vagina were free of tumor. Squamous morules and squamous differentiation with keratinization (Figure 2 and Figure 3) were noted.

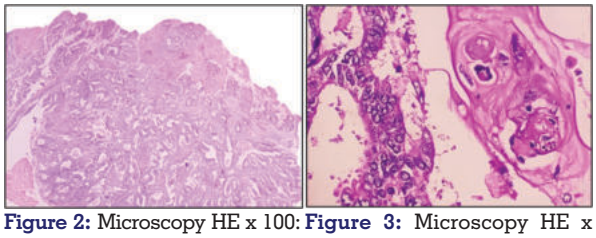

Figure 2: Microscopy HE x 100: Endometrioid adenocarcinoma with squamous morules and squamous differentiation with keratinization.

Figure 3: Microscopy HE x 400: Endometrioid adenocarcinoma with squamous differentiation with keratinization.

Surface of bilateral fallopian tubes (occasional left fimbrial mucosal aspect), parametria, surface of bilateral ovaries revealed giant cell reaction to degenerated keratinized cells, keratin material (keratin granuloma) with foci of ghost keratinized squamous cells. Neoplastic glandular or viable cells were not seen. Bilateral pelvic lymph nodes were uninvolved. Hence the final diagnosis was: Moderately differentiated endometrioid adenocarcinoma of uterus with squamous differentiation, FIGO grade 2, with involvement of cervix. However, as there was surface involvement of ovaries (Figure 4), fallopian tubes (Figure 5) and parametria, by keratin granuloma (Figure 6), a literature search of whether the tumor gets upstaged to pT3, was done. However, it was found that such reactions at various sites, doesn't change the stage or prognosis of the tumor. Hence the final stage of this tumour was pT2.

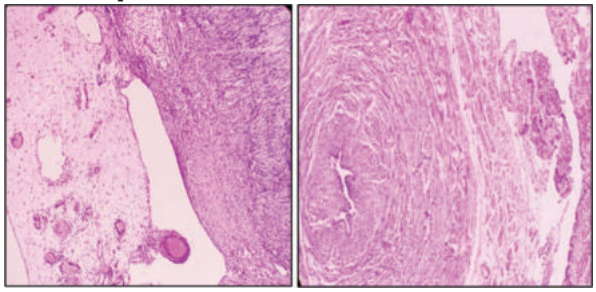

Figure 4: Microscopy HE x 100: Keratin granuloma on ovarian surface.

Figure 5: Microscopy HE x 100: Keratin granuloma on fallopian tube surface.

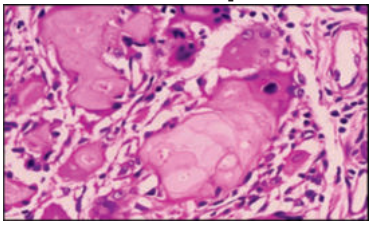

Figure 6: Microscopy HE x 400: Keratin granuloma.

DISCUSSION

Between 10 and 25% of endometrioid adenocarcinomas contain foci of squamous differentiation, which is recognized by keratin pearl formation, intercellular bridges or solid masses of cells with abundant, polygonal shaped, dense eosinophilic cytoplasm & distinct cell membranes. Squamous differentiation may be at the stromal interface or as morules, bridging adjacent glands. It is important to recognize squamous differentiation since it is not included in the estimation of solid growth for grading endometrioid adenocarcinoma.

FIGO stage, age, histological grade, depth of myometrial invasion and lymphovascular invasion are the most important predicators of lymph node involvement and outcome, and generally apply equally to endometrioid carcinoma and its variants with squamous, secretory & villoglandular differentiation.[3]

In 1961, Montes et al. reported a case of well differentiated adenocarcinoma of the uterine corpus with foreign body keratin granulomas, and named it "cholesteatomatous endometriosis". [4]

Histologically, keratin granulomas are composed of eosinophilic laminated keratin surrounded by multinucleated giant cells, histiocytes, lymphocytes and plasma cells. Keratin is associated with ghost squamous cells in which the nuclei have been lost. These keratin materials are speculated to be refluxed from the uterine tumor through the fallopian tubes toward the peritoneum because keratin clumps are often found within the lumen of the fallopian tubes. [5]

Keratin granulomas without viable cancer cells do not show any significant prognostic influence, although the number of cases is limited and the follow-up period is short. [6]

Peritoneal keratin granulomas without viable tumor cells do not influence the staging or the prognosis of the primary carcinoma. Therefore, they should not be regarded as an indicator of metastatic spread. [4,6-8]

CONCLUSION

Keratin granulomas at extrauterine sites with endometrioid adenocarcinoma of the uterus resemble dissemination of tumor grossly and microscopically. However, it is important to rule out neoplastic glandular cells in these granulomas, to entirely exclude metastasis/ dissemination. Keratin granulomas without tumor cells have no significant influences on the prognosis, although the number of these cases and the lengths of the follow-up period are limited.

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REFERENCES:

1. Mahdy H, Casey MJ, Crotzer D. Endometrial Cancer. [Updated 2022 Sep 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK525981/
2. K Chinen, K Kamiyama, T Kinjo, A Arasaki, Y Ihama, T Hamada, T Iwamasa. Morules in endometrial carcinoma and benign endometrial lesions differ from squamous differentiation tissue and are not infected with human papillomavirus. J Clin Pathol 2004;57:918–926.
3. R. Zaino, S.G. Carinelli et al. Tumours of the uterine corpus: Epithelial tumors and precursors. In: Robert J. Kurman, Maria Luisa Carcangiu, C. Simon Herrington, Robert H. Young, editors, WHO Classification of Tumours of Female Reproductive Organs.4th edition. Lyon: IARC; 2014
4. Montes M, Beautyman W, Haidak GL. Cholesteatomatous endometriosis. *Am J Obst & Gynec*. 1961;82:119–23.
5. Wotherspoon AC, Benjamin E, Boutwood AA. Peritoneal keratin granulomas from transtubal spread of endometrial carcinoma with squamous metaplasia (adenoacanthoma). Case report. *Br J Obstet Gynaecol*. 1989;96:236–40. doi: 10.1111/j.1471-0528.1989.tb01669.x.
6. Kim KR, Scully RE. Peritoneal keratin granulomas with carcinomas of endometrium and ovary and atypical polypoid adenomyoma of endometrium.
7. Chen KT, Kostich ND, Rosai J. Peritoneal foreign body granulomas to keratin in uterine adenoacanthoma. *Arch Pathol Lab Med*. 1978;102:174–7. [PubMed] [Google Scholar]
8. van der Horst C, Evans AJ. Peritoneal keratin granulomas complicating endometrial carcinoma: a report of two cases and review of the literature. *Int J Gynecol Cancer*. 2008;18:549–53. doi: 10.1111/j.1525-1438.2007.01033.x.